Differentiation of Progressive Brain Tumor from Radiation Injury: Utility of 1H MR Spectroscopy

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Introduction:
Radiosurgery is an important therapeutic modality for the treatment of malignant brain tumors, but increased local radiation doses are associated with an increased risk of radiation injury (leading to edema, rarefaction of white matter with reactive gliosis, transitory blood-brain barrier abnormalities or radiation necrosis). MRI features of these lesions are similar to those of progressive low- or high-grade brain tumors. 1H MR spectroscopy (MRS) proved to be sensitive and specific for the diagnosis of brain tumors [1-3]. The goal of this study was to evaluate the utility of single-voxel 1H MRS for differentiating recurrent or progressive tumor from post-irradiation tissue alterations.

Subjects and Methods:
A total of 70 combined MRI/MRS examinations have been performed in 43 patients at 1.5 T (SIEMENS Vision, Erlangen, Germany). All patients have been treated by radiosurgery for malignant brain tumors: Astrocytoma grade I (n=2), grade II (n=15), grade III (n=8), grade IV (n=5), oligodendroglioma grade II (n=4), grade III (n=3), and metastases (n=6). The decision for a MRS-examination was based on patient symptoms or suspicious MRI findings. After axial T1w and T2w spin-echo (SE) imaging localized, water-suppressed 1H MR spectra were obtained from 1 to 12 cm³ volumes centered in 51 lesions by using a PRESS sequence (TR=1500 ms, TE=135 ms). Contralateral control regions were examined in 32 patients. Multiplanar T1w SE images were obtained after administration of a paramagnetic contrast agent. Signal-time data were evaluated using a LPSVD algorithm. Relative signal intensities of choline-containing compounds (Cho), total creatine (Cr), N-acetyl aspartate (NAA), lactate, and free lipids were evaluated and statistical analysis was performed by using the nonparametric, unpaired Wilcoxon test.

Results and Discussion:
MRS could easily be incorporated into the MRI study protocol by adding only a few minutes examination time. Up to now, diagnoses were ensured in 33 patients (41 lesions) by clinical and MRI follow-up examinations, by PET or SPECT studies, or by biopsy. Recurrent or progressive tumors (PT) were found in 20 cases, no suspicious changes in tumor morphology (NC) in 11 cases and radiation injury (RI) in 10 lesions [gliosis/edema (n=5), transitory contrast enhancement (n=4), radiation necrosis (n=1)]. Significantly enhanced signal intensity ratios LCho/LCr (Fig. 1) and LCho/LNAA were observed in PT compared to NC (p=0.0001; p=0.0018) and RI lesions (p=0.0001; p=0.0006) as well as to contralateral control regions (p=0.0001; p=0.0001). No significant differences were found between the NC and RI lesions. Larger variations in the metabolite ratios were observed in PT lesions most probably reflecting different tumor histologies. LCho/LCr values larger than 2.5 were highly suspicious for progressive tumor. Values between ca. 1.5 and 2.5 overlap with those of radiation necrosis or transitory contrast enhancing lesions. In radiation necrosis high lipid levels were found. In two patients with radiation associated, transitory contrast-enhancing lesions, a continuous decrease of initially elevated LCho/LCr values were observed during follow-up (Fig. 2).

The positioning of the voxel(s) and the interpretation of the spectra must refer to clinical data and MRI findings and should be performed by an experienced neuroradiologist. In this case MRS will have a positive effect on further treatment decisions in terms of reduced additional diagnostic procedures (e.g., PET scanning or biopsy), increased patient comfort and reduced costs.

Fig. 1: Box plots of LCho/LCr, observed in lesions classified as progressive tumor (PT), no change (NC), radiation injury (RI); n.e.=not yet evaluated. Maximum value of data extend within three interquartile ranges (+) or more (*).

Fig. 2: Follow-up MRI/MRS examinations of a patient with astrocytoma grade II, who showed after radiosurgery a suspicious, contrast-enhancing lesion adjacent to the tumor. During follow-up T1w MR images showed a decrease of contrast medium uptake by the lesion (a, b) and simultaneously a decrease of LCho/LCr (c) indicating transitory blood-brain barrier alterations. The position of the MRS voxel is indicated (a,b).

References: